by Hallenbeck et al., U.S. Patent no. 5,998,205. Applicants respectfully submit that the presently claimed invention is not anticipated by the cited art.

The present claims are directed to a method of selective cytolysis of a target cell by a replication competent adenovirus vector, where an AFP-TRE directs expression of more than one adenoviral gene essential for replication.

The Hallenbeck patent is directed to targeted gene therapy. As stated in the summary of the invention, Hallenbeck et al. teaches the use of adenovirus as a vector for delivery genes, and therefore providing for expression in the tissue of interest. The concept of selective cytolysis is neither recited nor described in Hallenbeck, and is in fact contrary to the purposes of Hallenbeck, because selective cytolysis prevents expression of the heterologous gene product. Enhanced gene expression using cell specific regulatory elements, as described in Hallenbeck, actually teaches away from target cell lysis.

Hallenbeck *et al.* (5,998,205, filed 11/28/95) does not teach replication competent adenovirus vectors with more than one adenovirus gene essential for replication under control of a tissue-specific TRE, nor does it teach replication competent vectors for selective cytolysis of a target cell. In contrast, the specification of the present application clearly describes selective cytotoxicity on page 16, lines 17-20.

In view of the above amendments and remarks, Applicants respectfully submit that the presently claimed invention meets the requirements of 35 U.S.C. 102(e). Withdrawal of the rejection is requested.

CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is requested. If the Examiner finds that a Telephone Conference would expedite the prosecution of this application, she is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any other fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, order number CELL006CIP.

Respectfully submitted,

Date: August 1, 2002

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Page 1, paragraph 1, please replace with the following rewritten paragraph.

--This application is the U.S. National Phase of international application PCT/US98/04084, filed on March 3, 1998, and a continuation in part of U.S. Serial No. 09/033,428, filed March 2, 1998 both of which claim[s]priority to U.S. provisional patent application 60/039,597, which was filed March [2] 3, 1997.--

Page 6, lines 1-2, replace with the following rewritten lines:

--about +82[7]2 of SEQ ID NO:1. In another embodiment, the AFP-TRE comprises a nucleotide sequence from about +1 to about +300 of SEQ ID NO:1.--

Page 33, lines 9-11, replace with the following rewritten lines:

--5,648,478), probasin (described in commonly owned patent application U.S. Ser. No. 60/039,762 and U.S. Serial No. [08/_____] 09/033,333 (attorney docket number 34802/2000700)), and human kallikrein 2 (described in commonly owned patent application U.S. Seri. No. [60/_____] 60/076,545) attorney docket number 34802/3000920) and U.S. Ser. No. 60/054,523).

Following the Claims, please add the following:

--ABSTRACT OF THE INVENTION

Replication competent adenoviral vectors specific for cells expressing alfa-fetoprotein (AFP) are provided. These replication-competetent adenoviral vectors comprise adenovirus genes essential for replication under the transcriptional control of an AFP-transcriptional regulatory element.--

IN THE CLAIMS

Please cancel claims 73-75, 85-87 and 94.

71. (amended) A method for conferring selective cytotoxicity on a target cell, said method comprising contacting a cell which allows an α fetoprotein transcription regulatory element (AFP-TRE) to function with an adenovirus vector comprising [an] more than one adenovirus gene essential for viral replication under transcriptional control of an AFP-TRE[, said FP-TRE comprising an enhancer from an AFP gene,] whereby the vector enters the cell and replicates.

72. (amended) The method of claim 71, wherein the adenovirus gene [of the adenovirus is an early gene] essential for replication is selected from the group consisting of E1A, E1B and E4.

76. (amended) The method of claim 71, wherein the AFP-TRE comprises an enhancer presented as nucleotides from about 1 to about 300 of SEQ ID NO:1.

77. (amended) The method of claim 71, wherein the AFP-TRE comprises an enhancer presented as nucleotides from about 300 to about 600 of SEQ ID NO:1.

78. (amended) The method of claim 71, wherein the AFP-TRE comprises an enhancer presented as nucleotides from about 1 to about 600 of SEQ ID NO:1.

79. (amended) The method of Claim 71, wherein said AFP-TRE further comprises a promoter from an AFP gene presented as nucleotides from about 600 to about 822 of SEQ ID NO:1.

80. (amended) The method of claim [9] 71, wherein the AFP-TRE comprises SEQ ID NO:1.

81. (amended) The method of claim [9] 71, wherein the AFP-TRE comprises SEQ ID NO:2.

82. (amended) The method of claim 71, wherein the adenovirus vector [further] comprises [an additional adenovirus gene essential for replication under the transcriptional control of a second AFP-TRE, said second AFP-TRE comprising an enhancer from an AFP gene] more than one adenovirus genes essential for replication under transcriptional control of the same AFP-TRE.

83. (amended) A method of suppressing tumor growth in an individual having an AFP-expressing tumor, comprising contacting the tumor cells with an adenovirus vector comprising [an] more than one adenovirus gene essential for replication under transcriptional control of an AFP-TRE, [said AFP-TRE comprising an enhancer form an AFP gene,] whereby the adenoviral vector transfects the tumor cells and replicates.

84. (amended) The method of claim [13] 83, wherein the more than one adenovirus gene[of the adenovirus vector is an early gene] essential for replication is selected from the group consisting of E1A, E1B and E4.

88. (amended) The method of claim [13] 83, wherein the AFP-TRE comprises an enhancer presented as nucleotides from about 1 to about 300 of SEQ ID NO:1.

89. (amended) The method of claim [13] 83, wherein the AFP-TRE comprises an enhancer presented as nucleotides from about 300 to about 600 of SEQ ID NO:1.

90. (amended) The method of claim [13] 83, wherein the AFP-TRE comprises an enhancer presented as nucleotides from about 1 to about 600 of SEQ ID NO:1.

91. (amended) The method of claim [13] 83, wherein the AFP-TRE further comprises a promoter from an AFP gene presented as nucleotides from about 600 to about 822 of SEQ ID NO:1.

92. (amended) The method of claim [21] 83, wherein the AFP-TRE comprises SEQ ID NO:1.

93. (amended) The method of claim [21] 83, wherein the AFP-TRE comprises SEQ ID NO:2.

Please add new claims 98-101.

98. (new) The method of claim 71, wherein said adenovirus vector comprises a silencer. (supported by specification at page 22, lines 22-24)

99. (new) The method of claim 71, wherein said adenovirus vector comprises genetic sequences encoding GM-CSF. (supported by specification at page 30, lines 22-25 and on page 31, lines 12-15)

100. (new) The method of claim 83, wherein said adenovirus vector comprises a silencer.

101. (new) The method of claim 83, wherein said adenovirus vector comprises genetic sequences encoding GM-CSF.

ABSTRACT OF THE INVENTION

Replication competent adenoviral vectors specific for cells expressing alfa-fetoprotein (AFP) are provided. These replication-competetent adenoviral vectors comprise adenovirus genes essential for replication under the transcriptional control of an AFP-transcriptional regulatory element.